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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Karin Bohnet et al.	Art Unit:	
Serial No.:	09/743,494	Examiner:	
Filed:	January 10, 2001		
Title:	GENES OF THE DEAD BOX PROTEIN FAMILY, THEIR EXPRESSION PRODUCTS AND USE		

Assistant Commissioner for Patents and Trademarks
Washington, D.C. 20231

SUBMISSION OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Applicants submit herewith the International Preliminary Examination Report corresponding to the above-referenced application. Applicants petition for any necessary extensions of time for submission of this document. In addition, if there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 1 March 2001

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1998/FO83 NP	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP99/04892	International filing date (*day/month/year*) 10 July 1999 (10.07.99)	Priority date (*day/month/year*) 22 July 1998 (22.07.98)
International Patent Classification (IPC) or national classification and IPC C12N 15/61		
Applicant AVENTIS RESEARCH & TECHNOLOGIES GMBH & CO. KG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11 January 2000 (11.01.00)	06 October 2000 (06.10.2000)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

International application No.
PCT/EP99/04892

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☒ the international application as originally filed.

☐ the description, pages 1-27, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 2, filed with the letter of 07 June 2000 (07.06.2000),
Nos. 1,3-24, filed with the letter of 17 August 2000 (17.08.2000).

☐ the drawings, sheets/fig 1/5-5/5, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 99/04892

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	7-24	**YES**
	Claims	1-6	**NO**
Inventive step (IS)	Claims	9-13	**YES**
	Claims	7-8, 14-24	**NO**
Industrial applicability (IA)	Claims	1-20, 23-24	**YES**
	Claims		**NO**

2. Citations and explanations

See supplemental box

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 99/04892

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

See supplemental box

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

The present application describes two new proteins, Hc1 and Hc2, which belong the group of DEAD-box proteins, nucleic acids that code for these proteins and possible applications of these proteins and nucleic acids.

Consequently, the designation "Hc1" relates to the protein with an amino acid sequence as per SEQ ID 14 or to a nucleic acid sequence as per SEQ ID 13. Similarly, the designation "Hc2" relates to a protein as per amino and nucleic acid sequences SEQ ID 16 and SEQ ID 15, respectively.

Re. Box I

Basis of the report

The amended claims filed on the 19 August 2000 (with the letter dated 17 August 2000) were taken as the basis for this examination report.

However, **Claim 2** was not acknowledged to be valid, since it claims "nucleic acids...and parts thereof with at least *25* nucleotides...". (However, the description of the amended claims in the covering letter refers to "22 nucleotides").

Nevertheless, this lacks foundation in the description, since the passage of text from the description cited in the covering letter (page 6, line 15) describes "a nucleic acid comprising at least approximately 20 nucleotides".

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

Consequently, the Claim 2 submitted with the letter of 19 August 2000 is not valid under PCT Article 41(2).

Consequently, the version of Claim 2 submitted on 9 June 2000 was used as basis for this examination report.

Re. Box IV

Lack of unity of invention

Although Hc1 and Hc2 belong to the group of DEAD-box proteins, sequence comparisons with other proteins from this group show a relationship between Hc1 and the sub-group of p68 and p72 proteins (D1, D2), whereas Hc2 appears to be more closely related to the eIF-4A proteins of different species.

Although, as specified under point V.6, the isolation from *Tetrahymena* contributes to the acknowledgement of an inventive step for both individual genes claimed in the present application, this fact is not a sufficient basis for combining the genes and the proteins Hc1 and Hc2 to produce an invention that meets the requirements of unity of invention, since no special technical feature (PCT Rule 13.2) can be seen in the isolation of different genes from *Tetrahymena*.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

Nor can the combination "RNA helicase from *Tetrahymena*" be considered a special technical feature, since the two genes belong to very different sub-groups of RNA helicases. Moreover, a number of different RNA helicases were already isolated from different organisms and clearly no novel technical effect is achieved with the feature whereby they are prepared from *Tetrahymena*.

Consequently, no common special technical feature pursuant to PCT Rule 13.2 is present and unity of invention is not established.

The present application therefore comprises the following two inventions:

1) gene and protein as per SEQ ID 13 and 14;
2) gene and protein as per SEQ 1D 15 and 16.

Re. Box V

The application does not meet the requirements of PCT Article 33, since **Claims 1-6** are **not novel** and **Claims 7-8 and 14-24** do **not involve an inventive step**.

1) Hereinafter reference is made to the following documents (the sequence of the documents corresponds to the sequence in which they are listed in the international search report):

D1: 'Schizosaccharomyces pombe p68 protein; p68

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

gene; RNA helicase' EMBL SEQUENCE DATABASE, 19 April 1991 (1991-04-19), XP002121699 Cambridge, UK & R.D. IGGO ET AL.: 'p68 RNA helicase: Identification of a nucleolar form and cloning of related genes containing a conserved intron in yeasts' MOL. CELL. BIOL., Vol. 11, No. 3, March 1991 (1991-03), pages 1326-1333, ASM WASHINGTON DC, US

D2: 'Human DEAD-box protein p72' EMBL SEQUENCE DATABASE, 5 October 1996 (1996-10-05), XP002121700 Cambridge, UK & G.M. LAMM ET AL.: 'p72: a human nuclear DEAD box protein highly related to p68' NUCLEIC ACIDS RESEARCH, Vol. 24, No. 19, 1996, pages 3739-3747, IRL PRESS LIMITED, OXFORD, ENGLAND

D3: 'A. thaliana mRNA for eucaryotic translation initiation factor 4A-2' EMBL SEQUENCE DATABASE, 20 November 1992 (1992-11-20), XP002121701 Cambridge, UK & A.M. METZ ET AL.: 'Sequences for two cDNAs encoding Arabisopsis thaliana eucaryotic protein synthesis initiation factor 4A' GENE, Vol. 120, 1992, pages 313-314, ELSEVIER SCIENCE PUBLISHERS, B.V., AMSTERDAM, NL;

D4: 'N. plumbaginifolia NelF-4A2 mRNA for nicotiana eucaryotic translation initiation factor 4A' EMBL SEQUENCE DATABASE, 24 October 1991 (1991-10-24), XP002121702 Cambridge, UK & G.W. OWTTRIM ET AL.: 'Divergent genes for translation initiation factor elF-4A are coordinately expressed in tobacco' NUCLEIC

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

ACIDS RESEARCH, Vol. 19, No. 20, 1991, pages 5491-5496, IRL PRESS LIMITED, OXFORD, ENGLAND

D8: "Saccharomyces cerevisiae TIF2 gene". EMBL SEQUENCE DATABASE, 17 Nov. 1988 (update 12 Nov. 1993) Accession No. X12814.

Novelty (PCT Article 33(2)

2) **Claim 1** relates to "nucleic acids that code for a RNA helicase with an amino acid sequence as per SEQ ID 14 and parts thereof with at least 20 nucleotides [...]".

Whilst parts of SEQ ID 13, of at least 20 nucleotides long, were not shown in the prior art, it must be noted that origin cannot be technically established on the basis of a nucleic acid fragment (definition of a product in terms of the method for its production).

Consequently, a nucleic acid as per the above wording is identical to "parts of a nucleic acid with at least 20 nucleotides coding for a *fragment* of an amino acid sequence as per SEQ ID 14".

As also explained in point V.5, parts of SEQ ID 14 of 21 amino acids in length are identical to already published sequences (D1). Consequently, nucleic acids of 63 nucleotides in length coding for a fragment of an amino acid sequence as per SEQ ID 14 have already been published.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

Claim 1 is therefore not considered novel.

3) As specified in Box VIII, the scope of protection of Claim 2 also extends to parts of nucleic acids that code for fusion proteins and therefore also to nucleic acids that are wholly unrelated to the present invention. Claim 2 therefore also covers parts of *any* nucleic acid with at least 20 nucleotides, which is not considered novel.

4) Furthermore, the scope of protection of Claim 2 extends to the nucleotide sequence as per SEQ ID 13 and parts thereof with at least 20 nucleotides. Although the nucleotide sequences described in D3 and D4 are 60 and 63.4% identical to SEQ ID 15, as well as related identical nucleotide sequences of 14 and 18 bp, document D8, which describes the *Saccharomyces cerevisiae* TIF2 gene, shows a related identical nucleotide sequence of 21 bp.

This also falls within the scope of protection of Claim 2. For these reasons, Claim 2 cannot be considered novel.

5) By publishing the nucleic acid sequences as per Claims 1 and 2, the technical features of Claims 3 and 6 are already implicitly covered. Claims 3 and 6 are therefore not novel.

6) As also stated in point V.2, the origin of an isolated nucleic acid sequence cannot be derived

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

from the sequence itself. The technical feature relating to the origin of an already known nucleic acid from an alternative organism does not, therefore, represent a distinguishing feature.

Consequently, Claims 4 and 5 are not novel.

7) Although Claims 7 and 8 represent standard methods, they are not described as such in the prior art and can be considered novel.

8) Documents D1 and D2 describe proteins of an amino acid sequence that are, respectively, 59.2 and 56.8% identical to SEQ ID 14 and related identical sequences of 21 and 17 amino acids, respectively.

Claim 9 can therefore be considered novel.

9) The same applies to Claim 10, since the proteins of documents D3 and D4 are, respectively, 59.2 and 61.2% identical to SEQ ID 16 and have related identical sequences of 10 amino acids.

10) Since Claim 11 refers to the novel Claims 9 and 10, a method as per Claim 11 can also be considered novel.

11) Antibodies and the production thereof as per Claims 12 and 13, respectively, can also be considered novel. Although it is probable that antibodies directed against numerous already known

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

p68, p72 and elF-4A proteins also react with the present proteins, this cannot be clearly shown at the present time.

12) The subjects or methods as per Claims 14-24 are also based on nucleic acids of Claims 1-6, which do not satisfy the requirement for novelty.

Nevertheless, the prior art does not explicitly show such subjects or methods. Claims 14-24 are therefore considered novel.

Inventive step (PCT Article 33(3))

13) The production of an expression vector as per Claim 7 and a method for the production of a nucleic acid as per Claim 8 are standard methods. With regard to the use or production of sequences that do not satisfy the requirement for novelty, no inventive step can be acknowledged.

14) The methods for cloning the claimed genes Hc1 and Hc2 are standard methods that do not involve an inventive step, since the PCR primers used for isolation purposes represent only degenerated sequences of the already described p68/p72 or elF-4A genes. The technical problem of interest therefore consists merely in preparing an alternative organism for isolating corresponding genes.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

Tetrahymena is a commonly used model organism in this field. Although the cloning of corresponding proteins from *Tetrahymena* is obvious to a person skilled in the art, none of the prior art documents expressly refers to the genus *Tetrahymena* or to the group of ciliates. The proteins of Claims 9 and 10 and a method for the production thereof as per Claim 11 could therefore be considered inventive.

15) Accordingly, an inventive step can also be acknowledged for the preparation of antibodies and a method for the production thereof, as per Claims 12 and 13, respectively.

16) Whilst the subjects and methods of Claims 14-24 can be considered novel, no inventive step can be acknowledged. Said claims also relate to possible uses of nucleic acids of Claims 1-6, which do not satisfy the requirement for novelty. These uses are already known for similar genes, proteins, or fragments of these genes or proteins (as also stated in the actual application, for example page 2, line 22 - page 4, line 6) or represent standard uses.

Moreover, since the applicant is not able to demonstrate any technical effect produced by the use of the nucleic acids or peptides as per the present claims in contrast to already known uses of similar genes or proteins, Claims 14-24 do not involve an inventive step.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

Industrial applicability

17) The subject matter of Claims 21 and 22 also covers its application for medical treatment. The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of these claims. Patentability can also depend on the wording of the claims. The EPO, for example, does not recognise industrial applicability of claims to the use of a compound in a medical treatment; it does, however, allow claims to the first use of a known compound in a medical treatment or to the use of such a compound in the manufacture of a drug for a new medical treatment (see PCT Rule 67.1(iv)).

According to the wording of Claim 2, the scope of protection of that claim also extends to parts with at least 20 nucleotides of a nucleic acid "that codes for an RNA helicase [...] *or functional variants thereof*". This could not, however, be examined, since, in line with the definition of "functional variants" (page 12, line 19 - page 13, line 11), such a variant could, for example, also be a fusion protein *containing* SEQ ID 16 or a protein that is approximately 70% identical to SEQ ID 16. Part of a nucleic acid that codes for such a fusion protein can therefore also be from this region, which codes for the fusion partner, and therefore completely different from SEQ ID 15, for example. This cannot be considered novel.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I, IV.3, V.2 & VIII

The same applies to parts of a nucleic acid which code, for example, for a protein that is 70% identical to SEQ ID 14; it would not be possible to examine such a claim given the large number of possibilities.